With two noted exceptions, Wright is cited by the Examiner for disclosing all the limitations of the claimed decoy probes. Specifically, the Examiner acknowledges that Wright does not disclose (i) a second nucleotide base recognition sequence region ("second region") which is joined directly to the 5' end of the first nucleotide base recognition sequence region ("first region") or which is joined to the 3' end or the 5' end of the first region by a non-nucleotide linker; or (ii) a molecule lacking a terminal 3' OH group available to accept a nucleoside triphosphate in a polymerization reaction. Instead, the Examiner relies upon Kacian for disclosing a second region which is joined directly to the 5' end of the first region or to the 3' end or the 5' end of the first region by a non-nucleotide phosphorothioate linker. In support of this interpretation, the Examiner refers to the following sections of Kacian: Figures 1 and 2; column 6, line 54, to column 7, line 23; column 8, line 55, to column 9, line 32; and claim 21. *See* Final Action at page 4, paragraph 1.

Before remarking on the Examiner's reasons for this rejection, Applicants once again wish to stress two relevant features of the claimed decoy probes. First, the claim language requires that the second region be present in the decoy probe *if* the first region can be used to produce a functional double-stranded promoter sequence using a complementary oligonucleotide. Second, the claim language specifies that the second region may only be joined to the 3' end of the first region by means of a non-nucleotide linker. (The phrase "non-nucleotide linker" was used in the original claim language of parent application Serial No. 09/365,121 and is defined in the specification at page 6, lines 9-11.) Thus, if a prior art molecule includes a first region which can form a functional double-stranded promoter sequence with a complementary oligonucleotide, the Examiner must also identify a prior art reference which would suggest directly joining a second region to the 5' end of the first region or joining a second region to the 5' end or the 3' end of the first region by means of a non-nucleotide linker to make out a *prima facie* case of obviousness.

As discussed during the interview, Kacian discloses a first region capable of forming a functional double-stranded promoter sequence with a complementary oligonucleotide. *See* Kacian

at paragraph bridging columns 8 and 9 ("the modified promoter-primer does not contain a different recognition sequence (promoter) from the unmodified promoter-primer"). Kacian also discloses a second region joined directly to the first region which is capable of complexing with a target nucleic acid sequence. What the Examiner has not identified is any teaching or suggestion in Kacian alone or in combination with Walker of a blocked promoter-primer including a second or "primer" sequence which is joined to a first or "promoter" sequence by means of a non-nucleotide linker.

The Examiner's arguments suggest that Kacian teaches that the second region may be joined to the first region by means of a "non-nucleotide" phosphorothioate linker. *See* Final Action at paragraph bridging pages 8 and 9. In response, Applicants note that the only references to "phosphorothioate" in Kacian appear in Example 9 and in claims 19, 35, 37 and 40, and in each instance the reference is to a 3' terminal phosphorothioate deoxyribonucleotide. Nowhere, however, does Kacian suggest *joining* the first region (promoter) and second region (primer) using a non-nucleotide linker. This is an important distinction which was not rebutted during the interview.

For the reasons presented, Applicants submit that claims 1-16 are fully patentable in view of the cited references when those references are considered alone or in combination.

Claims 17 and 18 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Wright *et al.* (*Science* (1997) 26:614-617) in view of Kacian *et al.* (U.S. Patent No. 5,554,516), and further in view of Olson *et al.* (U.S. Patent No. 5,861,273). Applicants respectfully traverse this rejection for the reasons that follow.

Wright and Kacian are cited in combination for teaching the decoy probe of claims 1-16 for the reasons set forth in section 2 of the Examiner's Final Action. While concluding that neither Wright nor Kacian teaches a nucleotide base recognition sequence region having nucleotide base similarity of at least 75% with at least one of SEQ ID Nos. 1, 2, 3, 4, 5 and 6, the Examiner

nevertheless contends that the sequence of SEQ ID NO:3 of the presently claimed invention is identical to the sequence of SEQ ID NO:4 of Olson. Applicants submit that any showing of sequence similarity between the sequences of the claimed invention and Olson would be inadequate to overcome the deficiencies noted above in the combined teachings of Wright and Kacian. Accordingly, Applicants submit that claims 17 and 18 are fully patentable in view of the cited references when those references are considered alone or in combination.

Claims 34 and 35 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Wright *et al.* (*Science* (1997) 26:614-617) in view of Kacian *et al.* (U.S. Patent No. 5,554,516), and further in view of Dattagupta (U.S. Patent No. 5,215,899). Applicants respectfully traverse this rejection for the reasons that follow.

Wright and Kacian are cited in combination for teaching the decoy probe of claims 1-16 for the reasons set forth in section 2 of the Examiner's Final Action. Although concluding that Wright in view of Kacian do not teach a decoy probe containing a region of self-complementarity, the Examiner contends that Dattagupta teaches the decoy probe of the claimed invention having a region of self-complementarity. While Dattagupta does disclose a self-hybridizing probe capable of forming a double-stranded region which serves as a functional promoter, Dattagupta also clearly discloses that the two principal parts of the probe are joined together in a single polynucleotide. *See* Dattagupta at column 4, lines 27-53. The first part of the probe (A) includes self-hybridizing portions (a and a'), and the second part of the probe (B) is selected to hybridize to the target sequence. The first and second parts of Dattagupta's probe (A and B) are joined to each other directly or through an intervening sequence (b). Thus, like Wright and Kacian, Dattagupta fails to teach or suggest directly joining a second region to the 5' end of a first region or joining a second region to the 5' end or the 3' end of the first region by means of a non-nucleotide linker, where the first region can be used to produce a functional double-stranded promoter sequence. Accordingly,

Applicants submit that claims 34 and 35 are fully patentable in view of the cited references when those references are considered alone or in combination.

Conclusion

Applicants submit that the subject application is in condition for allowance and Notice to that effect is respectfully requested.

No fee is believed due in connection with this Reply. If Applicants are mistaken, please charge the amount due to Deposit Account No. 07-0835 in the name of Gen-Probe Incorporated.

Certificate of Transmission

At the Examiner's request, I hereby certify that this correspondence (and any referred to as attached) is being sent by facsimile to 703-746-4979, the Examiner's direct fax number, on the date indicated below to Box AF, Commissioner for Patents, Washington, D.C. 20231.

Respectfully Submitted,

Date: January 8, 2003 By: _____

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